REMARKS

The Office Action objected to the disclosure because pages 5 and 8 of the specification of the present patent application include amino acid sequences that are not in sequence compliance. Applicant has amended the specification to identify these sequences and correct these informalities. Applicant has also amended the specification by omitting a terminal amino group because it is understood that that the terminal amino acid has an amino group, and by omitting dashes between the amino acids. Applicant respectfully requests that the 'Sequence Listing' that is being submitted with the 'SUBMISSION OF "SEQUENCE LISTING," COMPUTER READABLE COPY, AND/OR AMENDMENT PERTAINING THERETO FOR BIOTECHNOLOGY INVENTION CONTAINING NUCLEOTIDE AND/OR AMINO ACID SEQUENCE' that accompanies this amendment be entered into the present patent application to comply with the 'NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES' that accompanied the present Office Action. Applicant is also submitting with this amendment an exact copy of this 'Sequence Listing' in computer readable form (CRF). No new matter has been added by these changes.

Claims 1-10 are currently pending in the present patent application. Claims 1-10 have been rejected.

According to the Office Action, "...claims 1-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Pirrung et al. (WO 90/15070). Pirrung et al teaches a method and device for preparing desired sequences on a substrate at known locations wherein bound material of the substrate is exposed to irradiation (pg. 10, lines 1-35) so as to activate material and permit binding (see abstract). The substrate has a variety of uses such as screening large numbers of peptides or receptors, wherein receptors are labeled with fluorescent markers for detection. Other applications of the invention include doping of organic material in the substrate (pg. 5, lines 14-36). In an alternative embodiment the surface may comprise of cage binding members that are capable of immobilizing receptors in predefined regions of a substrate for selective

activation that allow receptors that have differential affinity for one or more ligands to react (pg. 55, lines 30-37 and pg. 56, lines 1-11). A specific binding substance having a strong binding affinity for the binding member and a strong affinity for the receptor or a conjugate of the receptor may be used to act as a bridge between members and receptors if desired. The method uses a receptor prepared such that the receptor retains its activity toward a particular ligand (pg. 56 lines 30-36). According to Pirrung et al, receptors used in this method could be organic compounds such as polymers (oligomer), nucleic acids, peptides, drugs, cellular membranes, cells, etc. (pg. 11, lines 7-24). The binder molecule can be selected from the group consisting of agonists and antagonists for cell membrane receptors, oligonucleotides, nucleic acids, proteins, antibodies, etc. (pg. 9, lines 30-37)...".

Applicant has amended claim 1 to indicate that the receptors are exposed to X-ray radiation *after* they are exposed to potential binders. Support for this change can be found throughout the specification. See, for example, page 4, Detailed Description of the Invention, paragraph 1: "...a plurality of bead-supported receptors were exposed to at least one potential binder for a period of time sufficient for binding to occur, and then immobilized as an array onto a surface. Each member of the array was exposed to X-ray radiation. The detection of an X-ray fluorescence signal from a member of the array indicated that a binding event had occurred between that receptor and a binder...". See also page 8, last paragraph through the Table on page 9 for a more detailed description of specific examples using zirconium and a phosphate compound as potential binders for oligopeptides (first the receptors were exposed to zirconium and a phosphate compound, then immobilized onto a tacky dot™ plate in the form of an array, and then each member of the array was analyzed by X-ray fluorescence spectrometry). The Office Action has correctly pointed out that Pirrung et al. discloses irradiation of a bound substrate in order to permit binding to a binder. According to Pirrung et al., the substrate is first irradiated to remove protecting groups that interfere with binding, and then exposed to a binder. Pirrung et al. does not describe irradiating the substrate with X-rays after it has been exposed to a binder. By contrast, Applicant's claimed method involves irradiating the substrate after it has been exposed to a binder

to induce an X-ray fluorescent signal from any receptor where binding has occurred, and then detecting this X-ray fluorescent signal. Pirrung et al. does not appear to describe the use of X-rays to induce an X-ray fluorescent signal as a means of detecting binding between receptors and potential binders. Pirrung et al. does describe, and even require, the use of fluorescent markers because Pirrung et al uses light as an excitation source to induce a fluorescent signal. Pirrung et al. clearly have not realized that fluorescent markers are not necessary to observe fluorescence if X-ray radiation were used as an excitation source, as Applicant teaches and claimed in claim 1. Applicant has pointed out the advantages of using X-ray fluorescence instead of visible light as an excitation source (see page 13, last paragraph of the specification), one being that that potential binders tagged with fluorescent markers may exhibit altered binding properties as compared to untagged counterparts and that the binding properties of both tagged and untagged potential binders may be determined and compared by using the method of the present invention. Pirrung et al. requires fluorescent markers and therefore cannot make this type of comparison. For these reasons, Applicant believes that amended claim 1 is not anticipated by Pirrung et al. and respectfully requests that the rejection under 35 U.S.C. 102(b) to claim 1 be withdrawn.

Claims 2-8 and claim 10 depend from claim 1 and include all of the limitations of claim 1. Applicant believes that claim 1 is allowable and therefore that claims 2-8 and 10, which depend from claim 1, are also allowable. For these reasons, Applicant respectfully requests that the rejection under 35 U.S.C. 102(b) to claims 2-8 and claim 10 be withdrawn.

According to the present Office Action, "...claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pirrung et al in view of Weinberg et al. (USP#6,030,917). The teachings of Pirrung et al are set forth and is silent with respect to the binder being a metal ion. However, Weinberg et al. teaches methods of screening and characterization of libraries of organometallic compounds which can be used as catalysts and therapeutic agents (see abstract). Ancillary ligand-stabilized metal complexes are also useful as catalysts for reactions such as oxidation, reduction,

hydragenation, polymerization, carbonylation and other reactions. It would have been obvious to one of ordinary skill in the art to use the metal ion binder of Weinberg et al. in the method and device for preparing desired sequences on a substrate as taught by Pirrung et al. to screen for therapeutic agents and catalysts that are useful in oxidation, reduction and other useful reactions...". Applicant has amended claim 1 and believes that amended claim 1 is not anticipated by Pirrung et al. While Weinberg et al. teaches methods of screening and characterizing libraries of metal-containing compounds, the combination of Pirrung et al. and Weinberg et al. does not teach a method of preparing a library of receptors exposed to at least one potential binder and detecting binding between the receptors and potential binders using X-rays to induce and detect X-ray fluorescence signals to indicate that binding between a receptor and a binder has occurred. Claim 9 depends on and includes all of the limitations of amended claim 1. With the changes made to claim 1, Applicant believes that claim 9 is allowable over Pirrung et al. in view of Weinberg et al. For these reasons, Applicant respectfully requests that the rejection of claim 9 under 35 U.S.C. 103(a) be withdrawn.

Applicant respectfully requests that this amendment be entered into the present patent application.

For the reasons set forth above, Applicant believe that all currently pending claims are in condition for allowance, and such action at an early date is earnestly solicited. No new matter has been added by the above changes. Reexamination and reconsideration are respectfully requested.

Respectfully submitted,

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